PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference VA/H-32622A	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/07605	International filing date *(day/month/year)* 14.07.2003	Priority date *(day/month/year)* 15.07.2002
International Patent Classification (IPC) or both national classification and IPC A61K39/02		
Applicant NOVARTIS AG et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
16.01.2004	02.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Heiduschat, C Telephone No. +49 89 2399-7804

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/07605

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-14 as originally filed

Claims, Numbers

1-21 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☐ all parts.

   ☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-21
	No:	Claims	none
Inventive step (IS)	Yes:	Claims	1-6, 15-20
	No:	Claims	7-14, 21
Industrial applicability (IA)	Yes:	Claims	1-18
	No:	Claims	19-21

2. Citations and explanations

   see separate sheet

Re Item IV

Lack of unity of the invention

The International Searching Authority found three inventions in this international application. Please see International Search Report for details.
However, the present Authority considers that examination of all three inventions may be carried out without undue effort and according to rule 68.1 PCT does not invite the Applicant to restrict the claims or pay additional fees.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1) The Application
The present application is based on the use of Arthrobacter cells in the preparation of a medicament for treatment or prevention of piscirickettsiosis in fish.

2) The Prior Art
Reference is made to the following document/s/:

D1: WO-A-9833884
D2: Kuzyk MA et al. Vaccine, Butterworth Scientific. Guildford, Gb (21-03-2001), 19(17-19), 2337-2344
D3: WO-A-9611707
D4: Kuzyk MA et al., Infection And Immunity, (12-1996), 64(12), 5205-5210
D5: Koch C et al., Fems Microbiology Letters, Amsterdam, Nl (1994), 123(½), 167-171
D6: Gudding R et al., Journal Of Fish Diseases (05-2001), 24(4), 205-215
D7: JONES S R M: DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, KARGER, BASEL, CH, vol. 90, 1997, page 430 XP009016791 ISSN: 0301-5149

Live Arthrobacter has been used to prepare an immunostimulant or vaccine against infection by Renibacterium salmoninarum (D1), which is the causative agent of Bacterial Kidney Disease. Apparently Arthrobacter is very closely related to said infections agent (D5) and infects the same cell type without causing disease, but raising a protective immune response. Thus, it is considered by D1 as an alternative to other vaccines against BKD based on R. salmoninarum (see e.g. D3).
D2 and D4 describe the antigens of Piscirickettsia salmonis and an efficient subunit vaccine against this ricksettsial pathogen. This vaccine comprises a recombinantly produced 17kD lipoprotein OspA of P. salmonis. The strong protective immune response elicited by OspA is even augmented by incorporation of certain T Cell epitopes (TCE's) derived from tetanus toxin and measles virus as immunostimmulants. D6 describes the

developments in fish vaccinology. D7 discloses the immunostimmulatory effect of microbial extracts on fish inoculated with P. salmonis, without specifying the origin or the composition of said extracts.

3) Novelty
The specific vaccine or immunostimulatory compositions and their uses are considered novel over the prior art in the sense of Article 33(2) PCT.

4) Inventive Step

4.1 Claims 1 to 6 are directed to the use of Arthrobacter live cells in a medicament for treatment and prevention of piscirickettsiosis. As R. salmoninarum or Arthrobacter were not known to share any significant similarity in antigenicity with P. salmonis it cannot be considered obvious over the prior art that Arthrobacter can be used to induce immunity to said P. salmonis. Same applies to a method of treating or preventing piscirickettsiosis according to claim 20. Thus, the subject-matter of claims 1 to 6 and 20 is considered inventive in the sense of Article 33(3) PCT.

4.2 Claims 7 to 14 are directed to vaccine compositions comprising live Arthrobacter cells in combination with an immunostimmulant (claim 7, 12, 13) or an additional immunogen (claim 14), or killed Arthrobacter cell material (claims 8 to 11). Claim 21 is directed to the use of killed Arthrobacter cell material as immunostimmulant for fish. No reference is made to any particular infectious disease to be prevented by such a vaccine.

4.3 Document D1, which is considered to represent the most relevant state of the art, discloses a vaccine or immunostimulant based on live Arthrobacter.

4.4 The problem to be solved by the subject-matter of said claims may therefore be regarded as the provision of an alternative vaccine composition based on Arthrobacter. The solution provided by the Applicant is the combination of live Arthrobacter with further immunostimulatory or immunogenic components. However, this is considered obvious over the prior art.

4.5 D1 already described the use of live Arthrobacter as immunostimulatory agent and as component for a vaccine. It is considered as routine procedure to add immunostimulatory agents such as adjuvants or TCE's to vaccine compositions (see e.g. D2: p. 2341, right column, 2. paragraph; D6: p.206). The commonly used Complete Freud's Adjuvant for example comprises killed corynebacteria cell material (see Application p.3). The addition of further antigens, even of different pathogens, is also a common option in the design of vaccine compositions (e.g. D3: p.11; claim 2). The use of killed Arthrobacter as immunostimulant for fish (claim 21) is considered

as a routine modification of the live Arthrobacter that had already been suggested as immunostimulant and is therefore obvious over D1. At best the use the described vaccine for prevention of a specific disease other than the disease described in D1 may be considered as non-obvious (see also item 4.1).

4.6 Thus, in view of the combination of D1 with any of D2, D3 or D6. The subject-matter of claims 7 to 14 and 21 cannot be considered inventive in the sense of Article 33(3) PCT.

4.7 Claims 15 to 18 are based on specific vaccine compositions comprising both Arthrobacter and P. salmonis antigens. Claim 19 is directed to the use of a vaccine composition comprising live Arthrobacter and P. salmonis antigen according to claim 17 for protection against salmonid rickettsial septicaemia (SRS) and BKD. Vaccines to several fish pathogens are known in the art (D1 to D3; D6: p.207-209). Although also polyvalent vaccines are described in the prior art (e.g. D6: p.209, 3rd paragraph) no incentive is provided to combine antigens useful for vaccination against these two diseases in one vaccine composition. Thus, the specific combination according to claims 15 to 18 is considered as a non-obvious selection among a multiplicity of possible combinations of vaccines to different fish pathogens. Thus, the subject-matter according to claims 15 to 19 is considered inventive in the sense of Article 33(3) PCT.

5) Industrial Applicability

Claims 19 to 21 could be interpreted as being directed to a method of medical treatment. For the assessment of said claim on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.